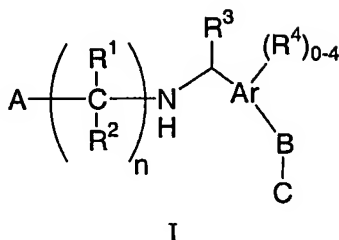


## WHAT IS CLAIMED IS:

1. A compound of Formula I



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

- 10 Ar is phenyl or naphthyl;

A is selected from:  $-\text{CO}_2\text{H}$ , 1*H*-tetrazol-5-yl,  $-\text{PO}_3\text{H}_2$ ,  $-\text{PO}_2\text{H}_2$ ,  $-\text{SO}_3\text{H}$ , and  $-\text{PO}(\text{R}^5)\text{OH}$ , wherein  $\text{R}^5$  is selected from the group consisting of:  $\text{C}_{1-4}$ alkyl, hydroxy $\text{C}_{1-4}$ alkyl, phenyl,  $-\text{C}(\text{O})-\text{C}_{1-3}$ alkoxy and  $-\text{CH}(\text{OH})$ -phenyl, said phenyl and phenyl portion of  $-\text{CH}(\text{OH})$ -phenyl optionally substituted with 1-3 substituents independently selected from the group consisting of: hydroxy, halo,  $-\text{CO}_2\text{H}$ ,  $\text{C}_{1-4}$ alkyl,  $-\text{S}(\text{O})_k\text{C}_{1-3}$ alkyl, wherein  $k$  is 0, 1 or 2,  $\text{C}_{1-3}$ alkoxy,  $\text{C}_{3-6}$  cycloalkoxy, aryl and aralkoxy, the alkyl portions of said  $\text{C}_{1-4}$ alkyl,  $-\text{S}(\text{O})_k\text{C}_{1-3}$ alkyl,  $\text{C}_{1-3}$ alkoxy and  $\text{C}_{3-6}$  cycloalkoxy optionally substituted with 1-3 halo groups;

20

$n$  is 2, 3 or 4;

each  $\text{R}^1$  and  $\text{R}^2$  is each independently selected from the group consisting of: hydrogen, halo, hydroxy,  $-\text{CO}_2\text{H}$ ,  $\text{C}_{1-6}$ alkyl and phenyl, said  $\text{C}_{1-6}$ alkyl and phenyl

- 25 optionally substituted with 1-3 halo groups;

$\text{R}^3$  is selected from the group consisting of: hydrogen and  $\text{C}_{1-4}$ alkyl, optionally substituted with 1-3 hydroxy or halo groups;

- 30 each  $\text{R}^4$  is independently selected from the group consisting of: hydroxy, halo,

-CO<sub>2</sub>H, C<sub>1-4</sub>alkyl, -S(O)<sub>k</sub>C<sub>1-3</sub>alkyl, wherein k is 0, 1 or 2, C<sub>1-3</sub>alkoxy, C<sub>3-6</sub>cycloalkoxy, aryl and aralkoxy, the alkyl portions of said C<sub>1-4</sub>alkyl, -S(O)<sub>k</sub>C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy and C<sub>3-6</sub>cycloalkoxy optionally substituted with 1-3 halo groups;

5 C is selected from the group consisting of:

- (1) C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, -(C=O)-C<sub>1-6</sub>alkyl or -CHOH-C<sub>1-6</sub>alkyl, said C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, -(C=O)-C<sub>1-6</sub>alkyl and -CHOH-C<sub>1-6</sub>alkyl optionally substituted with phenyl, and
  - (2) phenyl or HET, each optionally substituted with 1-3
- 10 substituents independently selected from the group consisting of: halo, phenyl, C<sub>1-4</sub>alkyl and C<sub>1-4</sub>alkoxy, said C<sub>1-4</sub>alkyl and C<sub>1-4</sub>alkoxy groups optionally substituted from one up to the
- 15 maximum number of substitutable positions with a substituent independently selected from halo and hydroxy, and said phenyl optionally substituted with 1 to 5 groups independently selected from the group consisting of : halo and C<sub>1-4</sub>alkyl, optionally substituted with 1-3 halo groups,

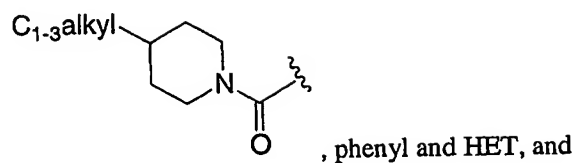
or C is not present;

20

when C is not present then B is selected from the group consisting of: phenyl, C<sub>5-16</sub>alkyl, C<sub>5-16</sub>alkenyl, C<sub>5-16</sub>alkynyl, -CHOH-C<sub>4-15</sub>alkyl, -CHOH-C<sub>4-15</sub>alkenyl, -CHOH-C<sub>4-15</sub>alkynyl, C<sub>4-15</sub>alkoxy, -O-C<sub>4-15</sub>alkenyl, -O-C<sub>4-15</sub>alkynyl, C<sub>4-15</sub>alkylthio, -S-C<sub>4-15</sub>alkenyl, -S-C<sub>4-15</sub>alkynyl, -CH<sub>2</sub>-C<sub>3-14</sub>alkoxy, -CH<sub>2</sub>-O-C<sub>3-14</sub>alkenyl, -CH<sub>2</sub>-O-C<sub>3-14</sub>alkynyl, -(C=O)-C<sub>4-15</sub>alkyl, -(C=O)-C<sub>4-15</sub>alkenyl, -(C=O)-C<sub>4-15</sub>alkynyl, -(C=O)-O-C<sub>3-14</sub>alkyl, -(C=O)-O-C<sub>3-14</sub>alkenyl, -(C=O)-O-C<sub>3-14</sub>alkynyl, -(C=O)-N(R<sup>6</sup>)(R<sup>7</sup>)-C<sub>3-14</sub>alkyl, -(C=O)-N(R<sup>6</sup>)(R<sup>7</sup>)-C<sub>3-14</sub>alkenyl, -(C=O)-N(R<sup>6</sup>)(R<sup>7</sup>)-C<sub>3-14</sub>alkynyl, -N(R<sup>6</sup>)(R<sup>7</sup>)-(C=O)-C<sub>3-14</sub>alkyl, -N(R<sup>6</sup>)(R<sup>7</sup>)-(C=O)-C<sub>3-14</sub>alkenyl and -N(R<sup>6</sup>)(R<sup>7</sup>)-(C=O)-C<sub>3-14</sub>alkynyl,

30

when C is phenyl or HET then B is selected from the group consisting of: C<sub>1-6</sub>alkyl, C<sub>1-5</sub>alkoxy, -(C=O)-C<sub>1-5</sub>alkyl, -(C=O)-O-C<sub>1-4</sub>alkyl, -(C=O)-N(R<sup>6</sup>)(R<sup>7</sup>)-C<sub>1-4</sub>alkyl,

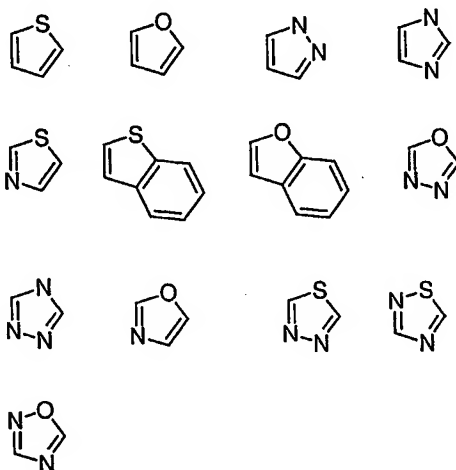


when C is C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, -(C=O)-C<sub>1-6</sub>alkyl or -CHOH-C<sub>1-6</sub>alkyl then B is  
 5 phenyl; and

R<sup>6</sup> and R<sup>7</sup> are independently selected from the group consisting of: hydrogen, C<sub>1-9</sub>alkyl and -(CH<sub>2</sub>)<sub>p</sub>-phenyl, wherein p is 1 to 5 and phenyl is optionally substituted  
 10 with 1-3 substituents independently selected from the group consisting of: C<sub>1-3</sub>alkyl and C<sub>1-3</sub>alkoxy, each optionally substituted with 1-3 halo groups.

2. The compound according to Claim 1 wherein HET is selected  
 from the group consisting of:

15



3. The compound according to Claim 1 wherein n is 2.
4. The compound according to Claim 1 wherein n is 3.

5. The compound according to Claim 3 wherein each R<sup>1</sup> and R<sup>2</sup> is independently selected from the group consisting of: hydrogen, -CO<sub>2</sub>H, hydroxy, halo, C<sub>1-3</sub>alkyl and phenyl.
- 5                    6. The compound according to Claim 1 wherein A is PO<sub>3</sub>H<sub>2</sub>.
7. The compound according to Claim 1 wherein A is -CO<sub>2</sub>H.
8. The compound according to Claim 1 wherein A is PO(R<sup>5</sup>)OH,  
10 wherein R<sup>5</sup> is selected from the group consisting of: C<sub>1-4</sub>alkyl, hydroxyC<sub>1-4</sub>alkyl, C(O)-C<sub>1-2</sub>alkoxy and benzyl, wherein both the methyl and phenyl portions of said benzyl are optionally substituted with 1-3 halo or hydroxy groups.
9. The compound according to Claim 1 wherein A is PO<sub>2</sub>H<sub>2</sub>.
- 15                   10. The compound according to Claim 1 wherein A is 1*H*-tetrazol-5-yl.
11. The compound according to Claim 1 wherein R<sup>3</sup> is hydrogen or  
20 methyl.
12. The compound according to Claim 1 wherein each R<sup>4</sup> is independently selected from the group consisting of: halo, hydroxy, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkylthio, phenyl, benzyloxy and cyclopropyloxy.
- 25                   13. The compound according to Claim 1 wherein B is C<sub>8-10</sub>alkyl and C is not present.
14. The compound according to Claim 1 wherein B is C<sub>4-11</sub>alkoxy  
30 and C is not present.
15. The compound of according to Claim 1 wherein B is phenyl, optionally substituted with 1-3 substituents independently selected from the group

consisting of: halo, C<sub>1-4</sub>alkyl and C<sub>1-4</sub>alkoxy, and C is selected from the group consisting of: hydrogen, phenyl, C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, -(C=O)-C<sub>1-6</sub>alkyl and -CHOH-C<sub>1-6</sub>alkyl, said C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkoxy, -(C=O)-C<sub>1-6</sub>alkyl and -CHOH-C<sub>1-6</sub>alkyl optionally substituted with phenyl.

5

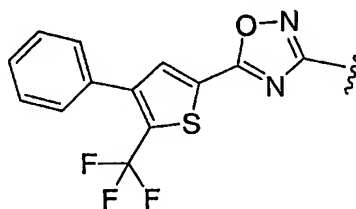
16. The compound according to Claim 1 wherein B is selected from the group consisting of: -CHOH-C<sub>6-10</sub>alkyl, C<sub>6-10</sub>alkylthio, -CH<sub>2</sub>-C<sub>5-9</sub>alkoxy, -(C=O)-C<sub>6-10</sub>alkyl, -(C=O)-O-C<sub>5-9</sub>alkyl, -(C=O)-N(R<sup>6</sup>)(R<sup>7</sup>)-C<sub>5-9</sub>alkyl, -N(R<sup>6</sup>)(R<sup>7</sup>)-(C=O)-C<sub>5-9</sub>alkyl, and C is not present.

10

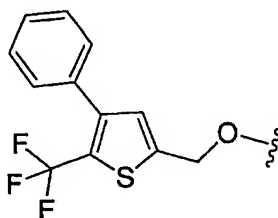
17. The compound according to Claim 1 wherein B is C<sub>1-6</sub>alkyl or C<sub>1-5</sub>alkoxy and C is phenyl.

18. The compound according to Claim 1 wherein B-C is

15



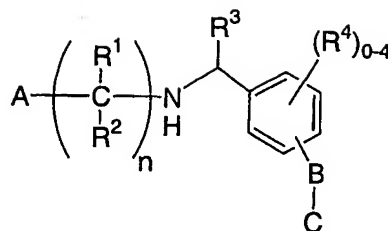
or



19. The compound according to Claim 1 wherein Ar is phenyl and the group -B-C is attached to the phenyl ring at the 3- or 4-position.

20

20. A compound of Formula II



II

or a pharmaceutically acceptable salt or hydrate thereof, wherein

5

the group -B-C is attached to the phenyl ring at the 3- or 4-position;

n is 2, 3 or 4;

each R<sup>1</sup> and R<sup>2</sup> is independently selected from the group consisting of: hydrogen, -  
10 CO<sub>2</sub>H, hydroxy, halo, C<sub>1</sub>-3alkyl and phenyl, said C<sub>1</sub>-3alkyl and phenyl optionally  
substituted with 1-3 halo group;

A is selected from the group consisting of: 1H-tetrazol-5-yl, PO<sub>2</sub>H<sub>2</sub>, PO<sub>3</sub>H<sub>2</sub>, -CO<sub>2</sub>H  
and PO(R<sup>5</sup>)OH, wherein R<sup>5</sup> is selected from the group consisting of: C<sub>1</sub>-4alkyl,  
hydroxyc<sub>1</sub>-4alkyl, C(O)-C<sub>1</sub>-2alkoxy and benzyl, wherein both the methyl and phenyl  
15 portions of said benzyl are optionally substituted with 1-3 halo or hydroxy groups;

R<sup>3</sup> is hydrogen or methyl;

each R<sup>4</sup> is independently selected from the group consisting of: halo, hydroxy, C<sub>1</sub>-  
20 3alkyl, C<sub>1</sub>-3alkoxy, C<sub>1</sub>-3alkylthio, phenyl, benzyloxy and cyclopropyloxy; and

B-C is selected from the group consisting of:

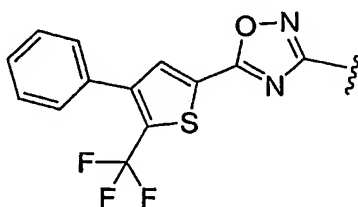
- (1) B is C<sub>8</sub>-10alkyl and C is not present.
- 25 (2) B is C<sub>4</sub>-11alkoxy and C is not present.
- (3) B is phenyl, optionally substituted with 1-3 substituents  
independently selected from the group consisting of: halo, C<sub>1</sub>-4alkyl and C<sub>1</sub>-4alkoxy,  
and C is selected from the group consisting of: hydrogen, phenyl, C<sub>1</sub>-8alkyl, C<sub>1</sub>-  
galkoxy, -(C=O)-C<sub>1</sub>-6alkyl and -CHOH-C<sub>1</sub>-6alkyl, said C<sub>1</sub>-8alkyl, C<sub>1</sub>-8alkoxy, -  
30 (C=O)-C<sub>1</sub>-6alkyl and -CHOH-C<sub>1</sub>-6alkyl optionally substituted with phenyl;

(4) **B** is -CHOH-C<sub>6-10</sub>alkyl, C<sub>6-10</sub>alkylthio, -CH<sub>2</sub>-C<sub>5-9</sub>alkoxy, -  
(C=O)-C<sub>6-10</sub>alkyl, -(C=O)-O-C<sub>5-9</sub>alkyl, -(C=O)-N(R<sup>6</sup>)(R<sup>7</sup>)-C<sub>5-9</sub>alkyl or -  
N(R<sup>6</sup>)(R<sup>7</sup>)-(C=O)-C<sub>5-9</sub>alkyl, and **C** is not present.

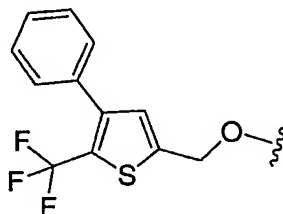
(5) **B** is C<sub>1-6</sub>alkyl or C<sub>1-5</sub>alkoxy and **C** is phenyl.

(6) **B-C** is

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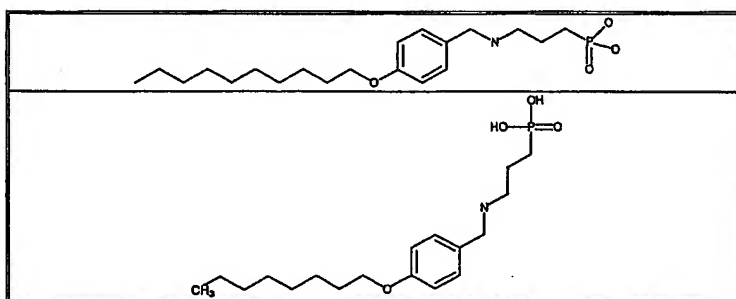


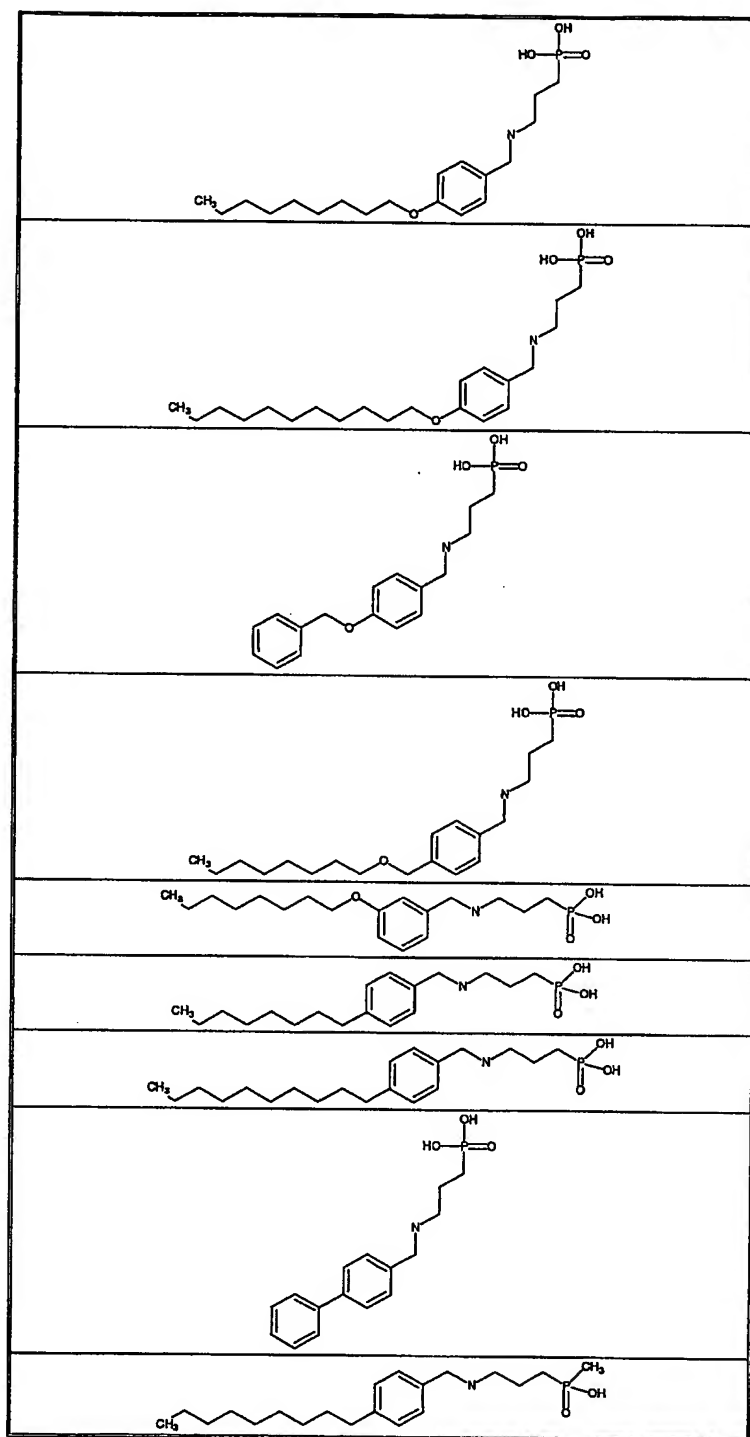
or



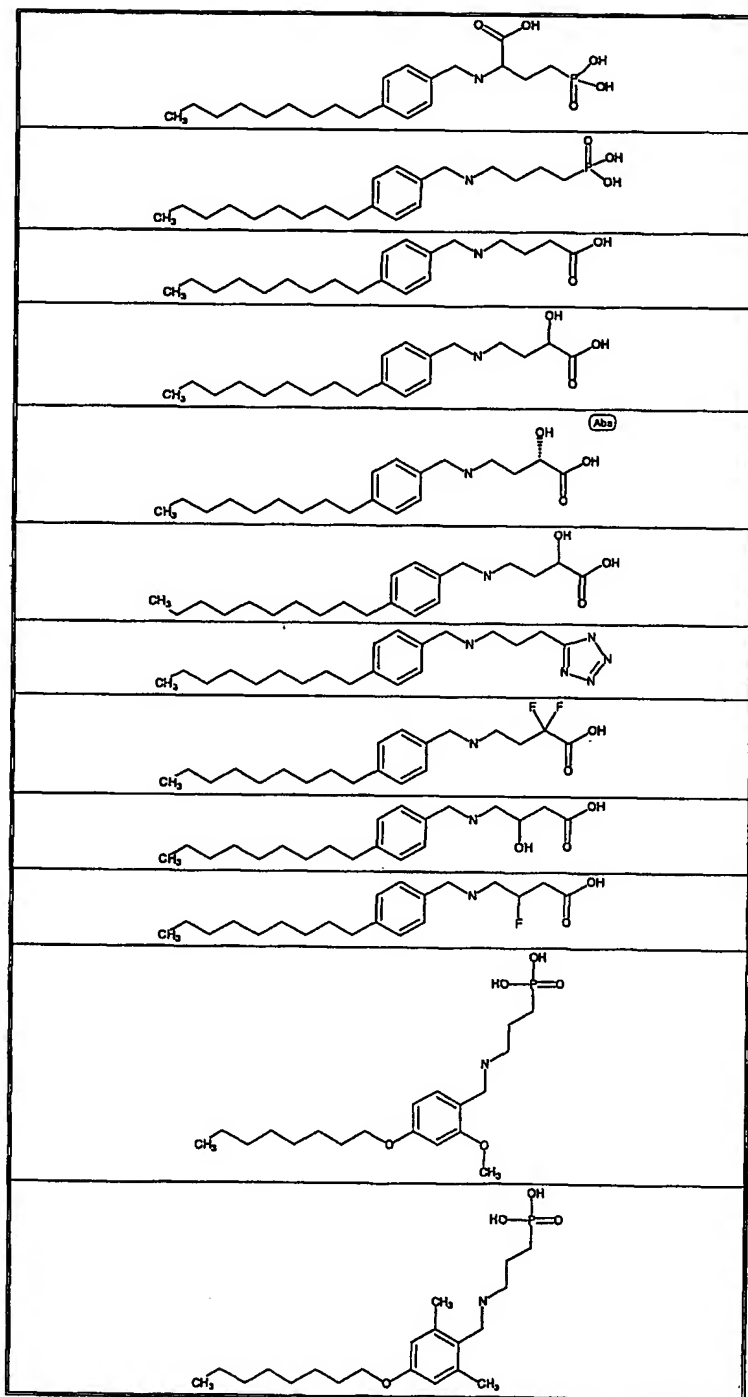
21. A compound selected from the group consisting of:

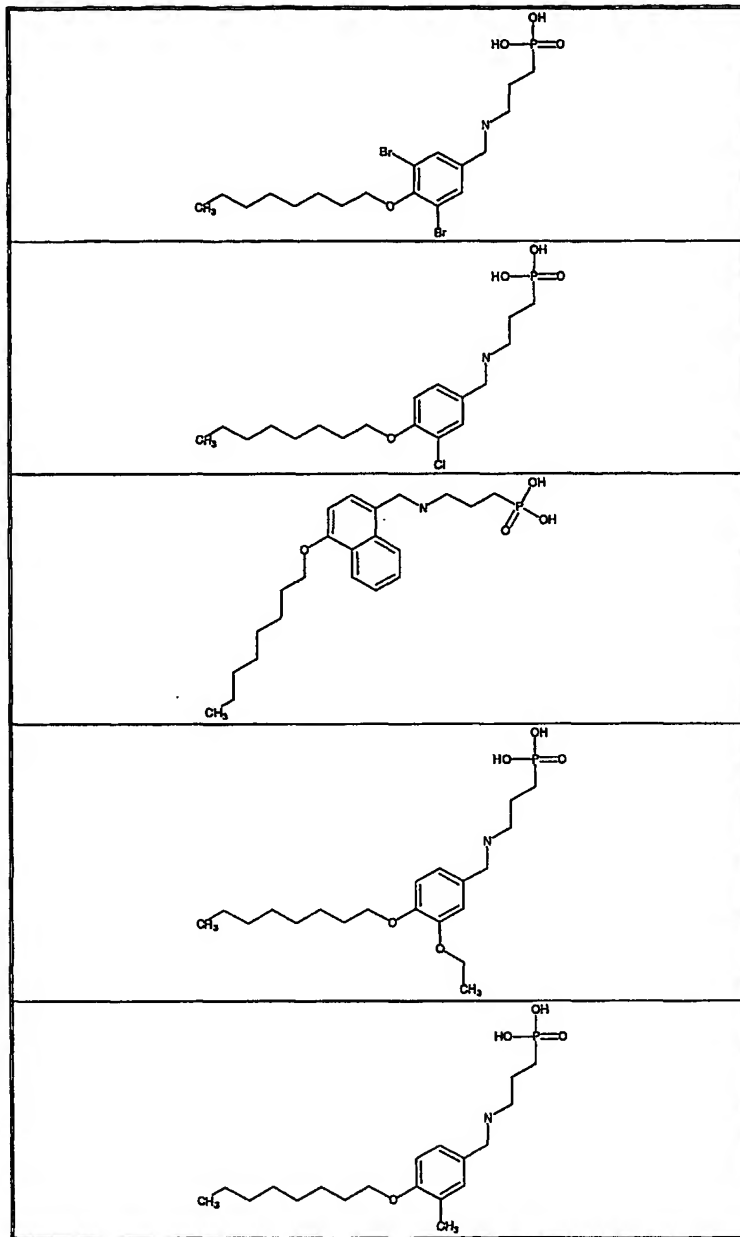
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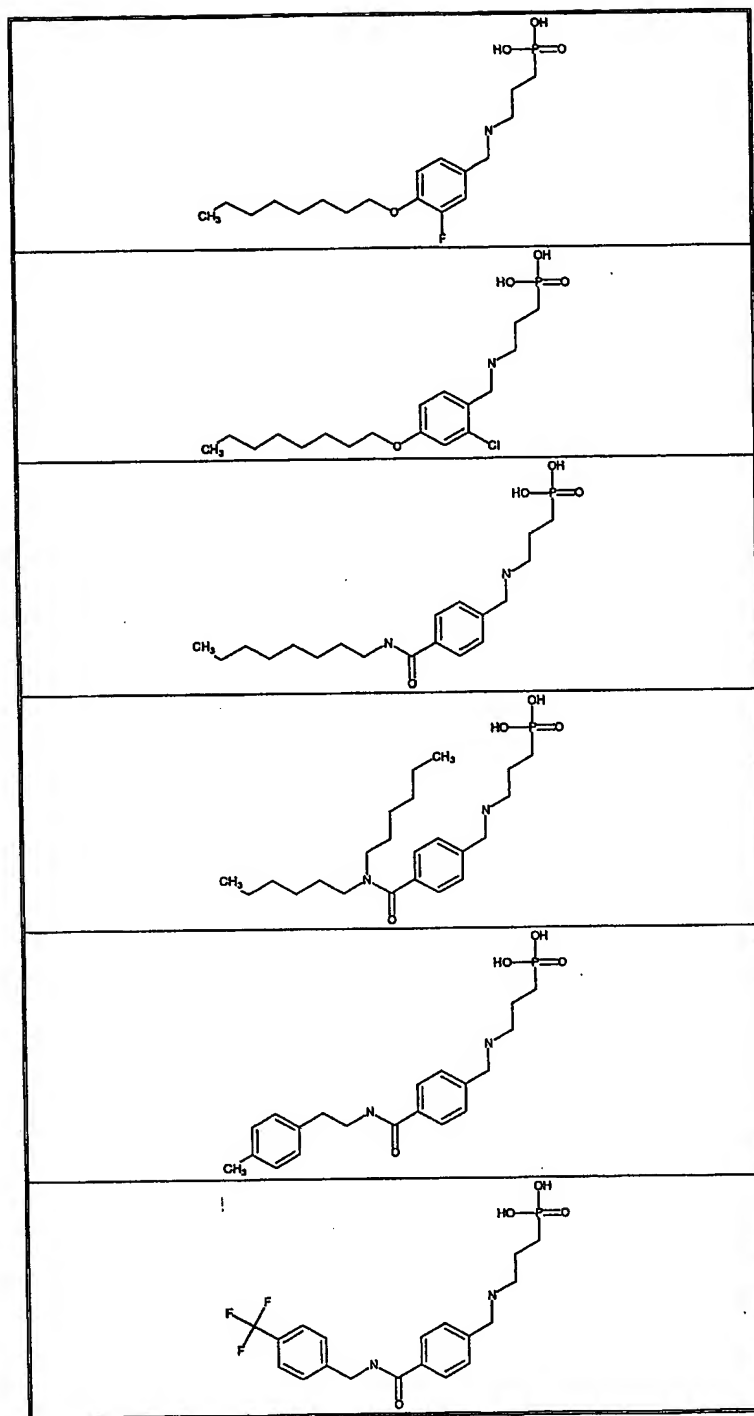




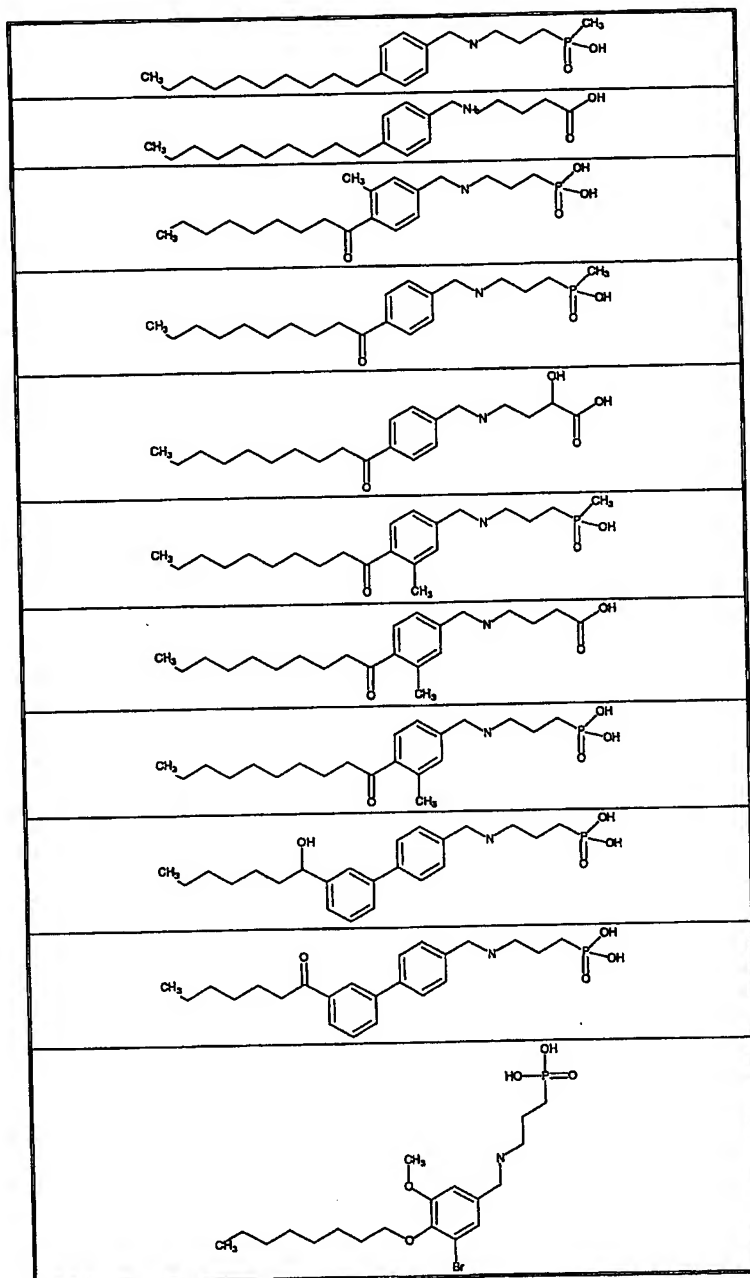


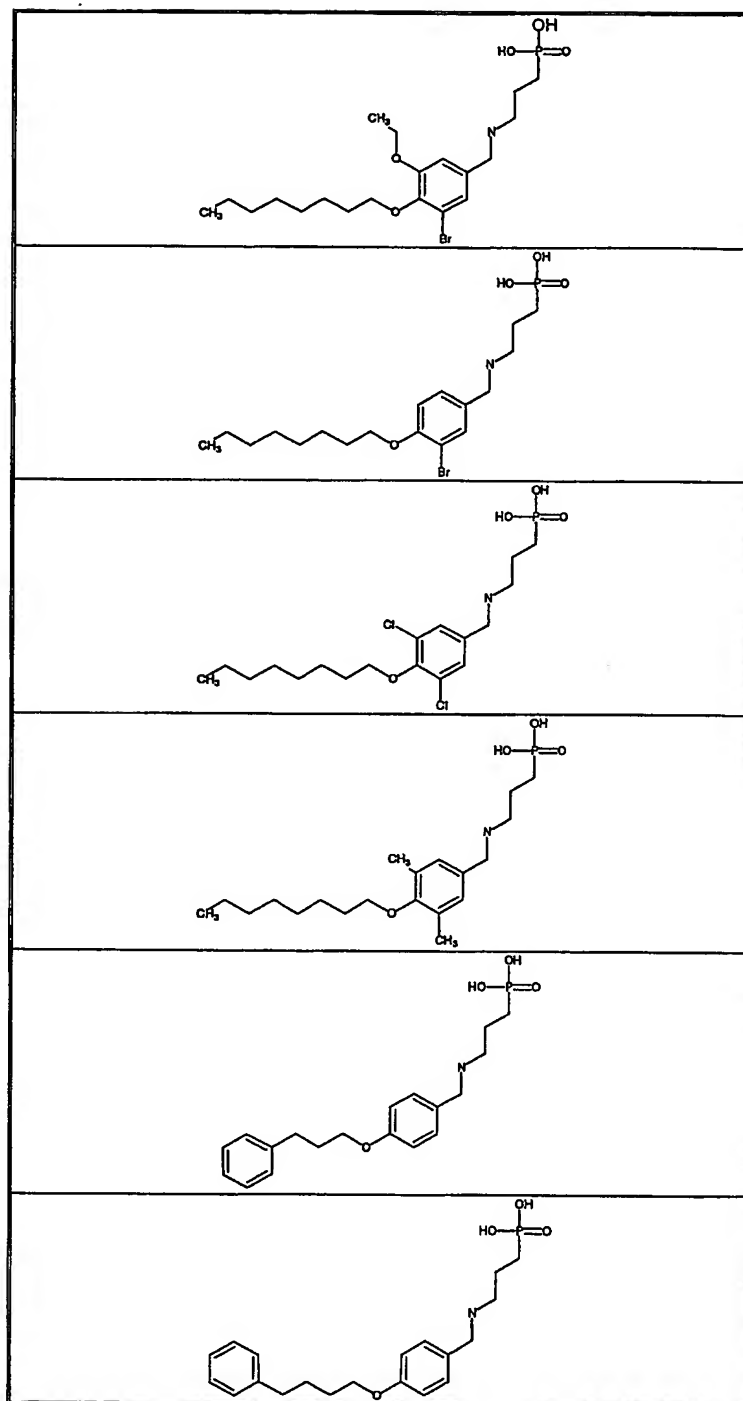




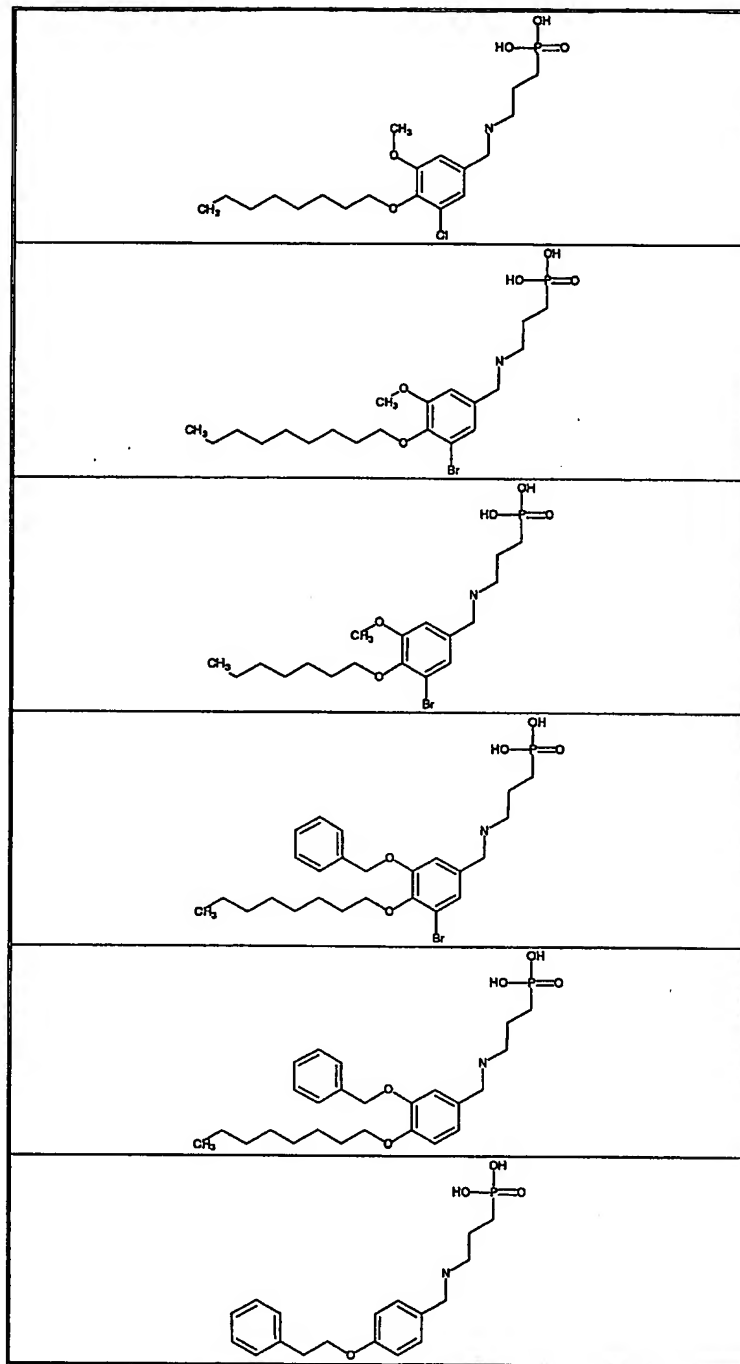




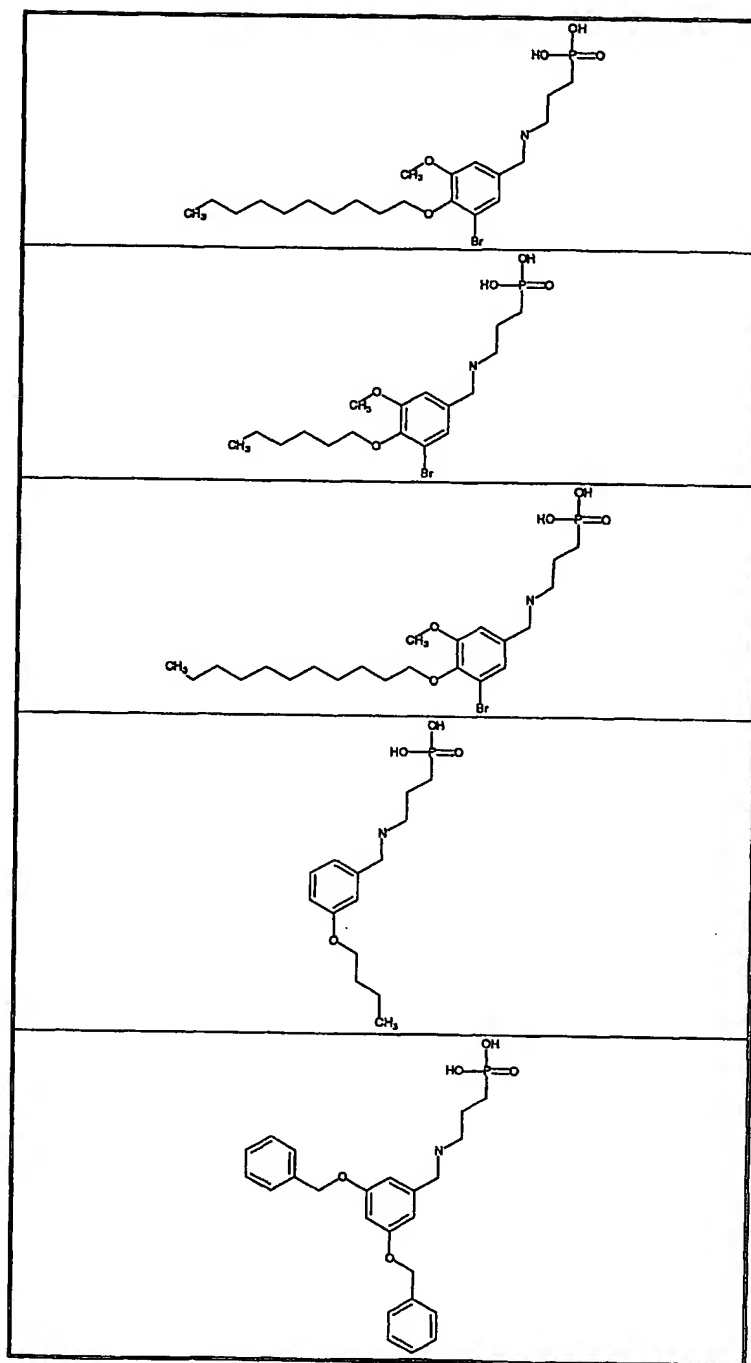


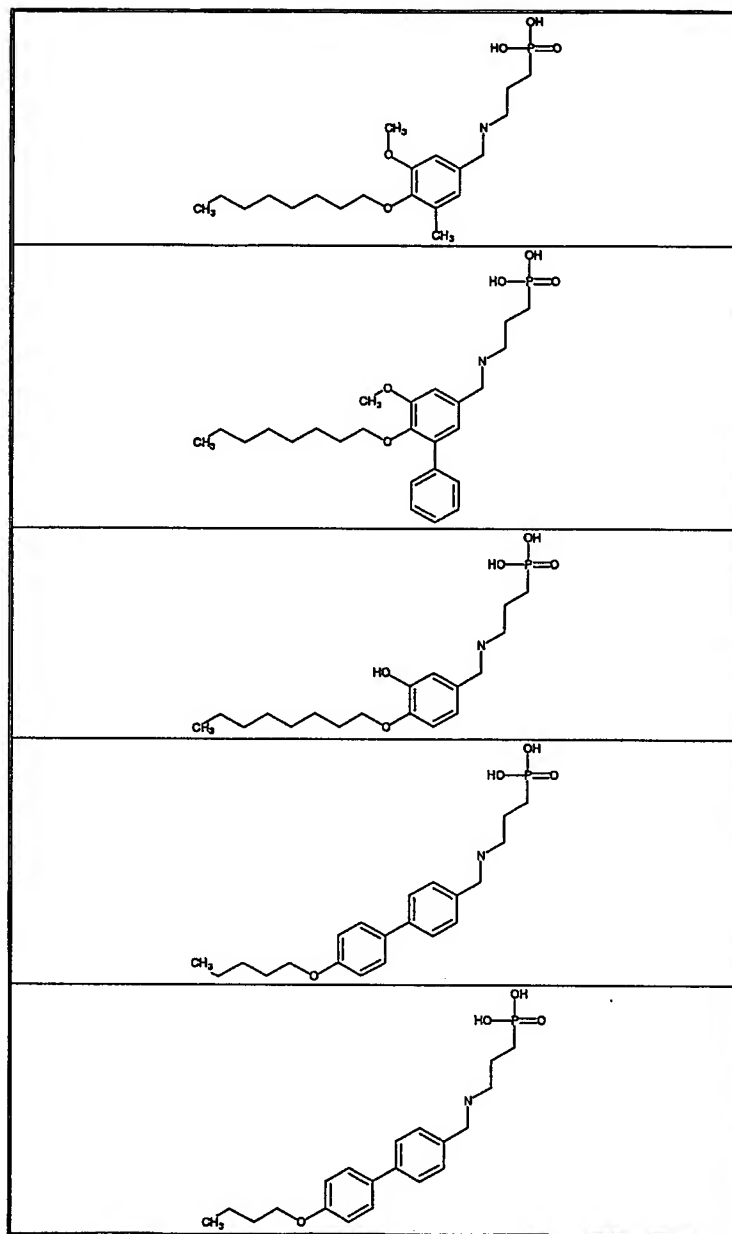


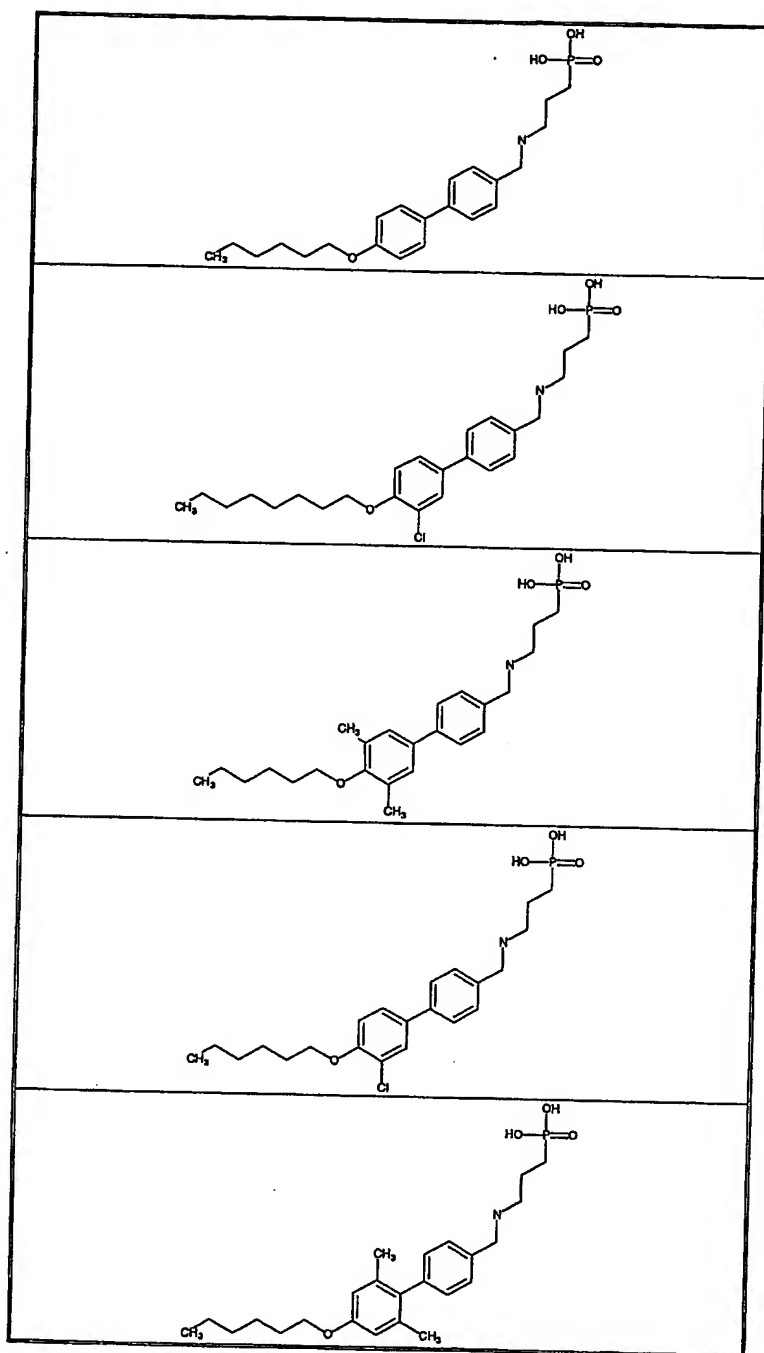




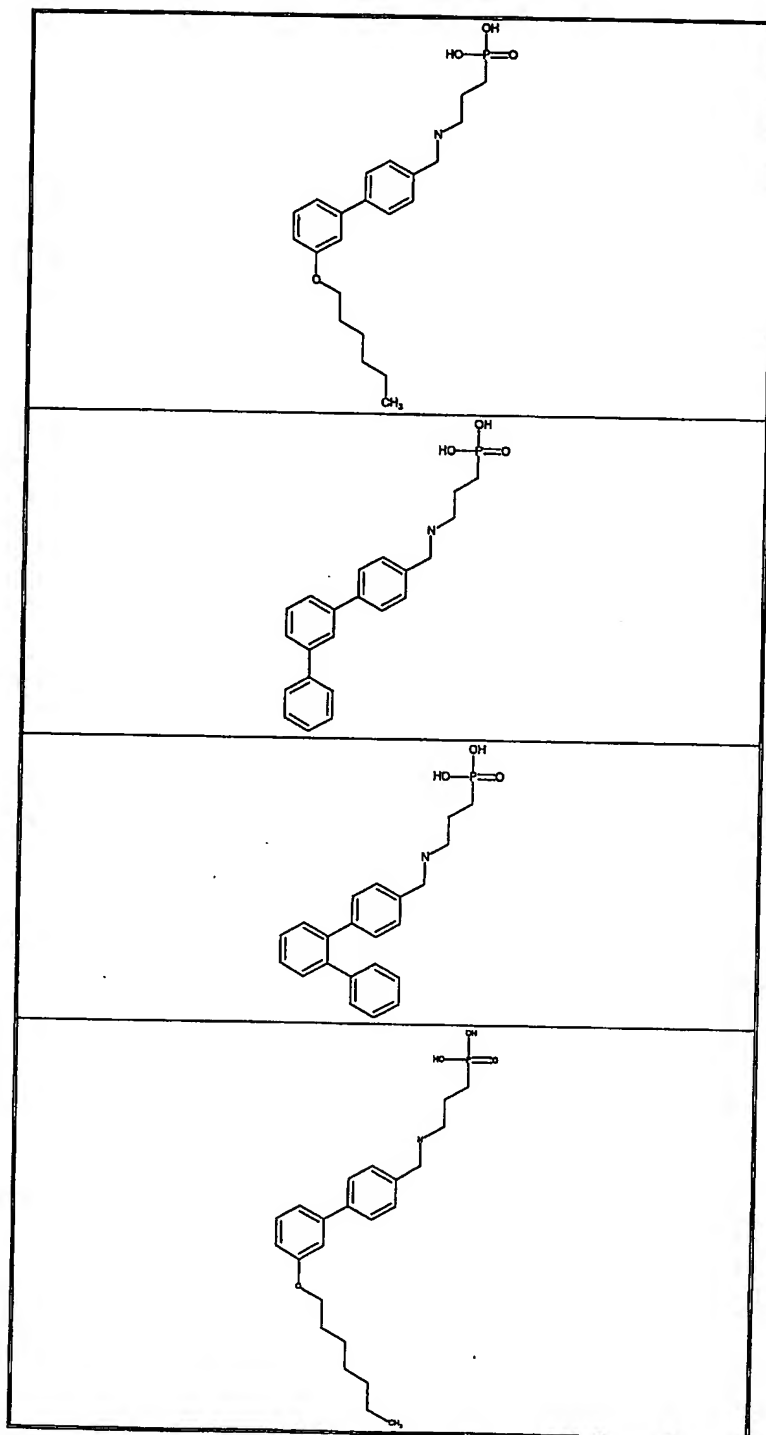


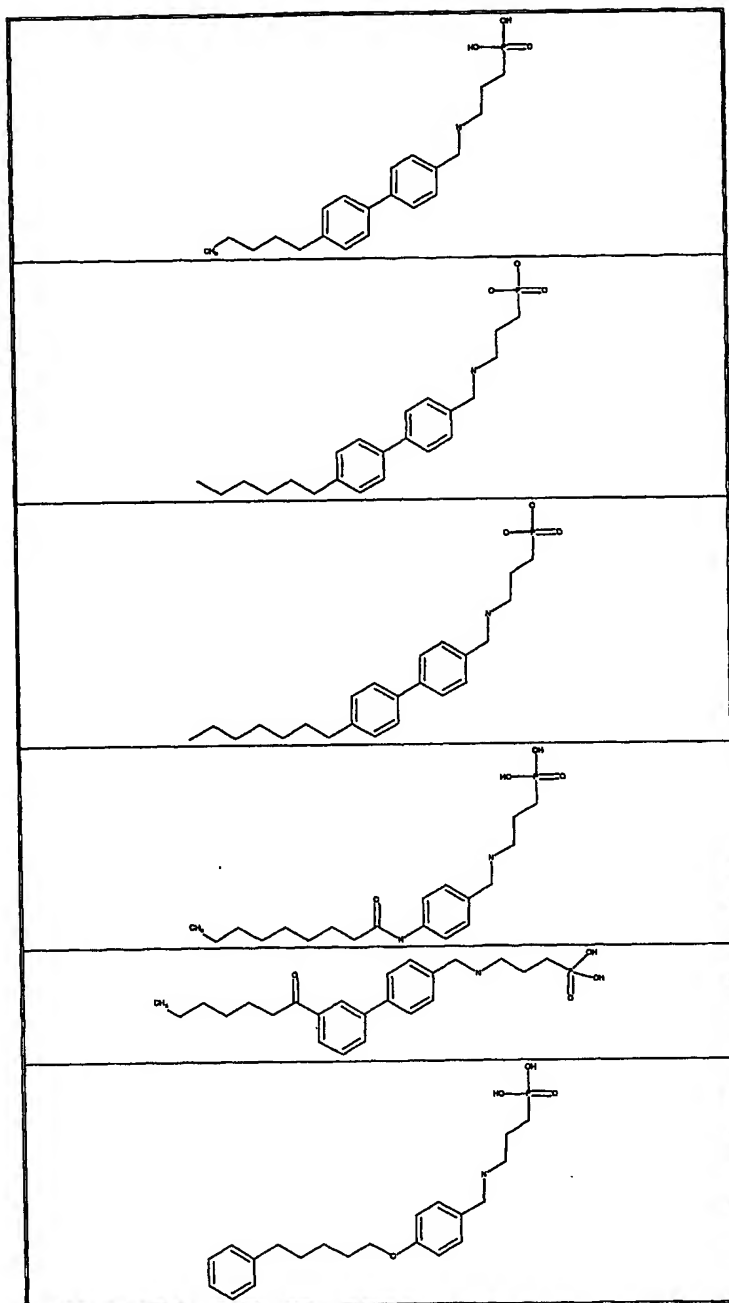


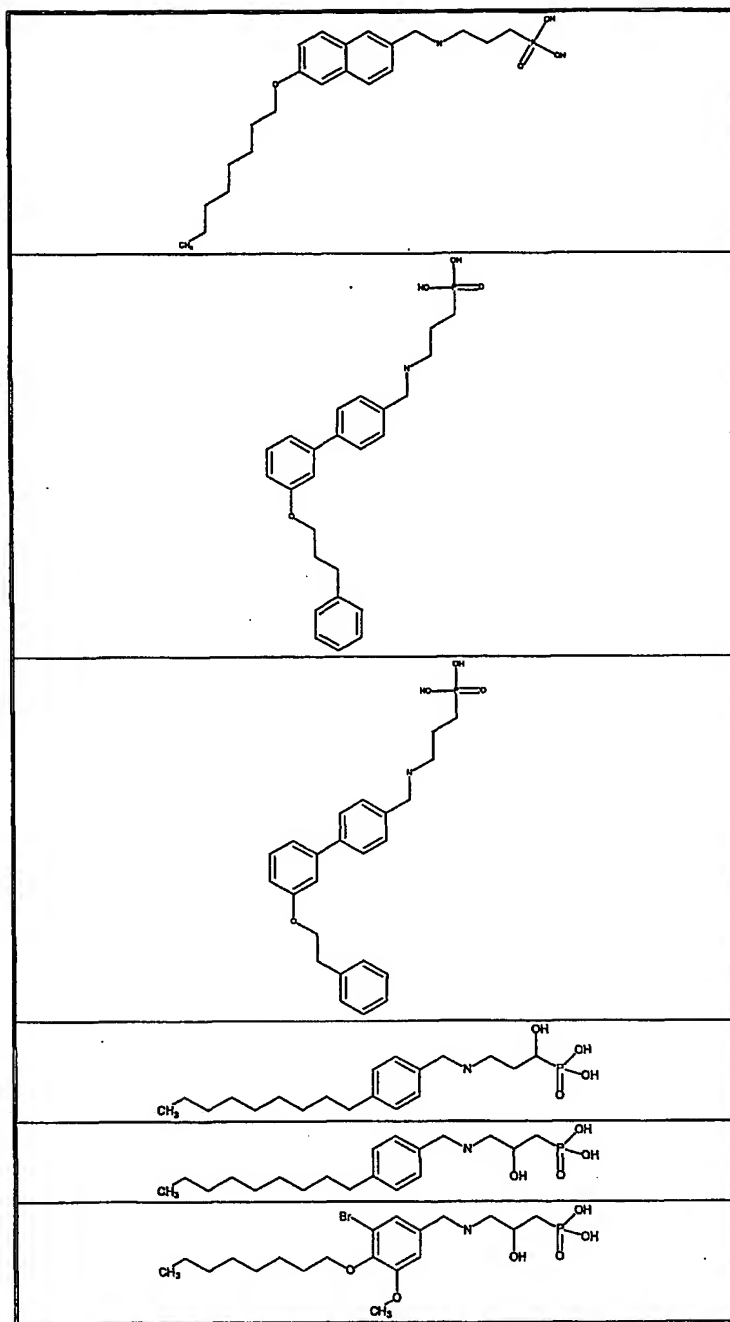


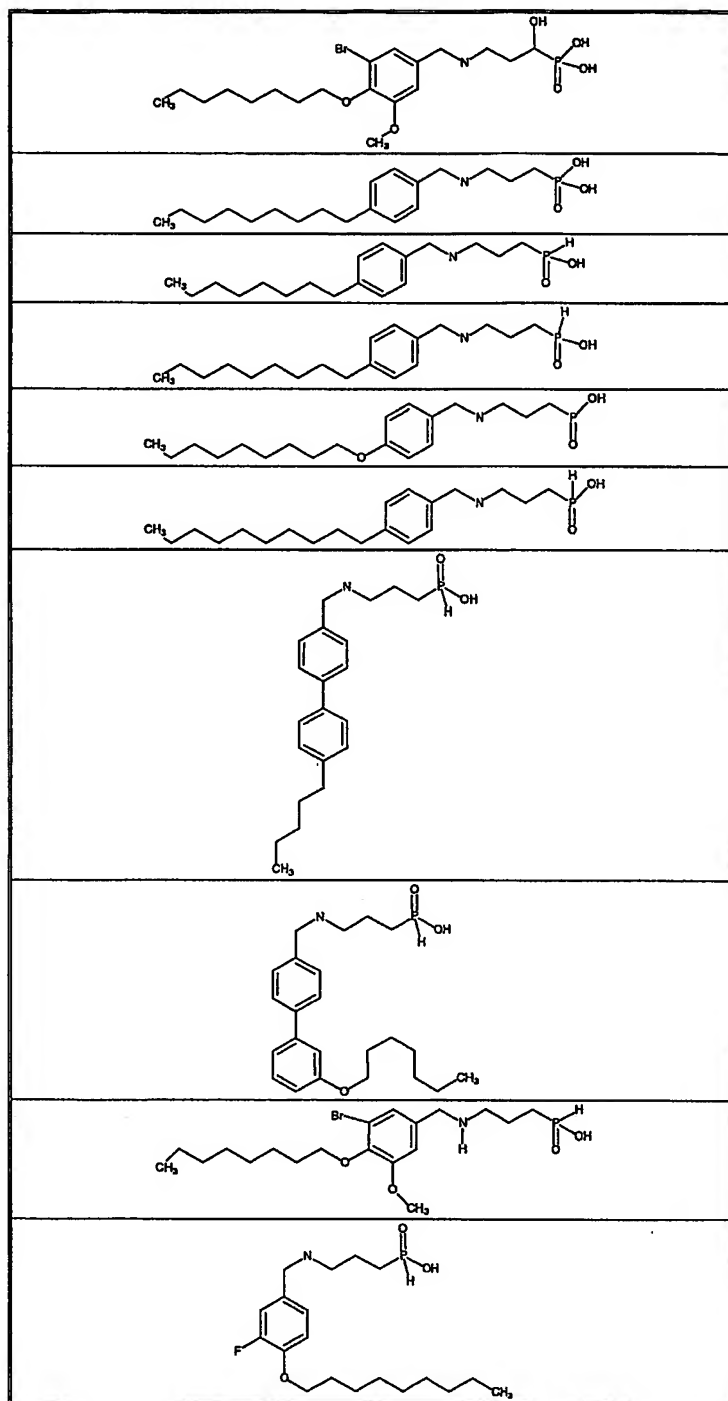




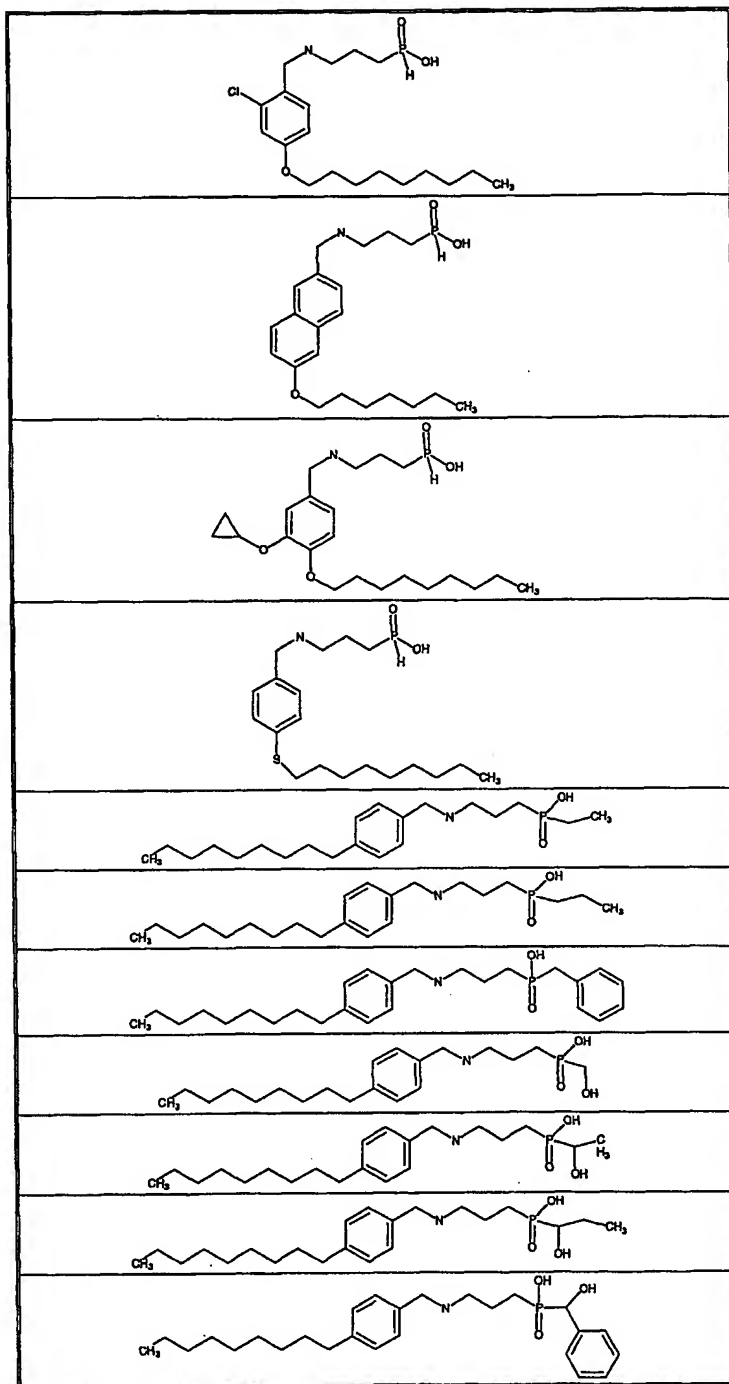


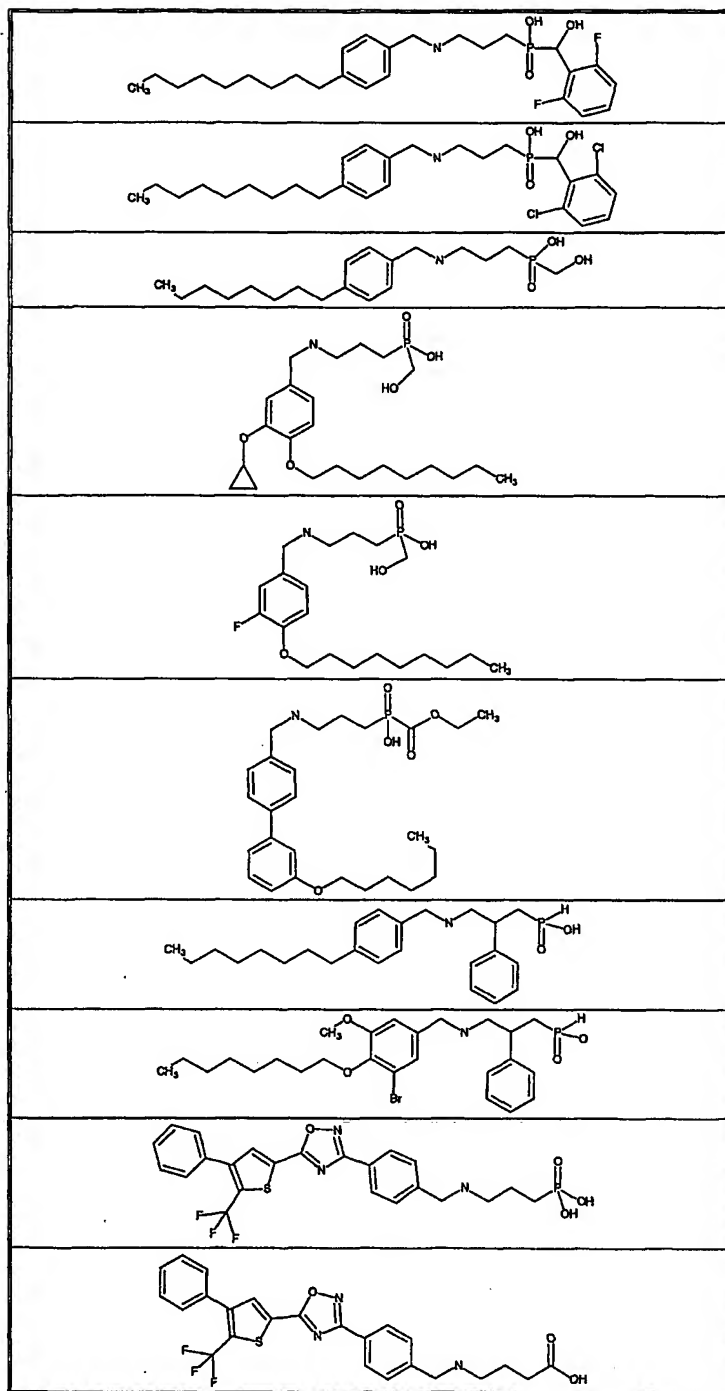


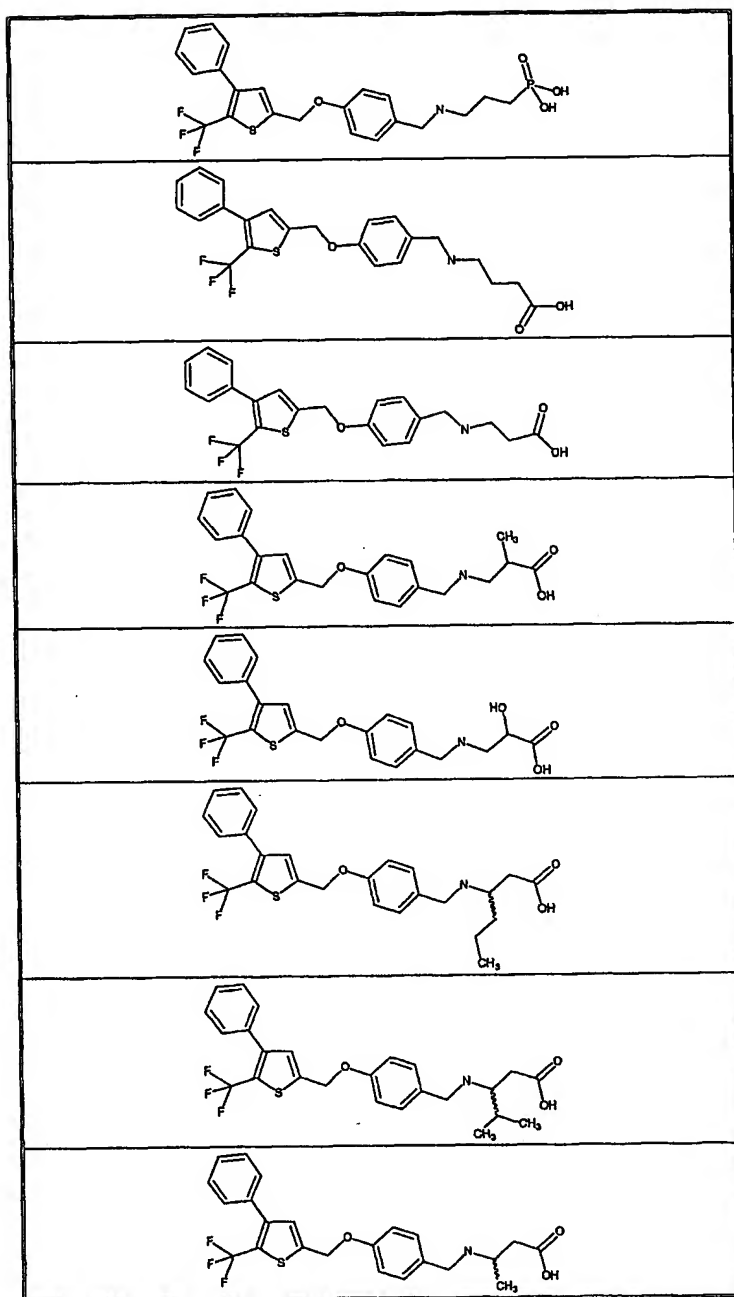


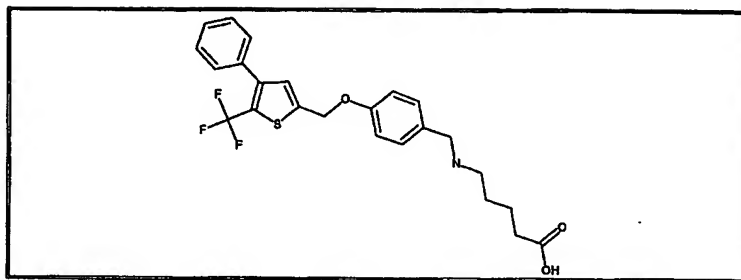












22. A method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound in accordance with Claim 1 in an amount that is effective for treating  
5 said immunoregulatory abnormality.

23. The method according to Claim 22 wherein the immunoregulatory abnormality is an autoimmune or chronic inflammatory disease selected from the group consisting of: systemic lupus erythematosus, chronic  
10 rheumatoid arthritis, type I diabetes mellitus, inflammatory bowel disease, biliary cirrhosis, uveitis, multiple sclerosis, Crohn's disease, ulcerative colitis, bullous pemphigoid, sarcoidosis, psoriasis, autoimmune myositis, Wegener's granulomatosis, ichthyosis, Graves ophthalmopathy and asthma.

15 24. The method according to Claim 22 wherein the immunoregulatory abnormality is bone marrow or organ transplant rejection or graft-versus-host disease.

25. The method according to Claim 22 wherein the  
20 immunoregulatory abnormality is selected from the group consisting of: transplantation of organs or tissue, graft-versus-host diseases brought about by transplantation, autoimmune syndromes including rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes, uveitis, posterior uveitis, allergic encephalomyelitis, glomerulonephritis,  
25 post-infectious autoimmune diseases including rheumatic fever and post-infectious glomerulonephritis, inflammatory and hyperproliferative skin diseases, psoriasis, atopic dermatitis, contact dermatitis, eczematous dermatitis, seborrheic dermatitis, lichen planus, pemphigus, bullous pemphigoid, epidermolysis bullosa, urticaria,

- angioedemas, vasculitis, erythema, cutaneous eosinophilia, lupus erythematosus, acne, alopecia areata, keratoconjunctivitis, vernal conjunctivitis, uveitis associated with Behcet's disease, keratitis, herpetic keratitis, conical cornea, dystrophia epithelialis corneae, corneal leukoma, ocular pemphigus, Mooren's ulcer, scleritis, Graves' ophthalmopathy, Vogt-Koyanagi-Harada syndrome, sarcoidosis, pollen allergies, reversible obstructive airway disease, bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, dust asthma, chronic or inveterate asthma, late asthma and airway hyper-responsiveness, bronchitis, gastric ulcers, vascular damage caused by ischemic diseases and thrombosis, ischemic bowel diseases, inflammatory bowel diseases, necrotizing enterocolitis, intestinal lesions associated with thermal burns, coeliac diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, Crohn's disease, ulcerative colitis, migraine, rhinitis, eczema, interstitial nephritis, Goodpasture's syndrome, hemolytic-uremic syndrome, diabetic nephropathy, multiple myositis, Guillain-Barre syndrome, Meniere's disease, polyneuritis, multiple neuritis, mononeuritis, radiculopathy, hyperthyroidism, Basedow's disease, pure red cell aplasia, aplastic anemia, hypoplastic anemia, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, agranulocytosis, pernicious anemia, megaloblastic anemia, anerythroplasia, osteoporosis, sarcoidosis, fibroid lung, idiopathic interstitial pneumonia, dermatomyositis, leukoderma vulgaris, ichthyosis vulgaris, photoallergic sensitivity, cutaneous T cell lymphoma, arteriosclerosis, atherosclerosis, aortitis syndrome, polyarteritis nodosa, myocarditis, scleroderma, Wegener's granuloma, Sjogren's syndrome, adiposis, eosinophilic fascitis, lesions of gingiva, periodontium, alveolar bone, substantia ossea dentis, glomerulonephritis, male pattern alopecia or alopecia senilis by preventing epilation or providing hair germination and/or promoting hair generation and hair growth, muscular dystrophy, pyoderma and Sezary's syndrome, Addison's disease, ischemia-reperfusion injury of organs which occurs upon preservation, transplantation or ischemic disease, endotoxin-shock, pseudomembranous colitis, colitis caused by drug or radiation, ischemic acute renal insufficiency, chronic renal insufficiency, toxinsosis caused by lung-oxygen or drugs, lung cancer, pulmonary emphysema, cataracta, siderosis, retinitis pigmentosa, senile macular degeneration, vitreal scarring, corneal alkali burn, dermatitis erythema multiforme, linear IgA ballous dermatitis and cement dermatitis, gingivitis, periodontitis, sepsis, pancreatitis, diseases caused by environmental pollution, aging, carcinogenesis, metastasis of carcinoma and hypobaropathy, disease caused by histamine or leukotriene-C4 release, Behcet's disease, autoimmune hepatitis, primary

biliary cirrhosis, sclerosing cholangitis, partial liver resection, acute liver necrosis, necrosis caused by toxin, viral hepatitis, shock, or anoxia, B-virus hepatitis, non-A/non-B hepatitis, cirrhosis, alcoholic cirrhosis, hepatic failure, fulminant hepatic failure, late-onset hepatic failure, "acute-on-chronic" liver failure, augmentation of  
5 chemotherapy effect, cytomegalovirus infection, HCMV infection, AIDS, cancer, senile dementia, trauma, and chronic bacterial infection.

26. The method according to Claim 22 wherein the  
immunoregulatory abnormality is multiple sclerosis  
10

27. The method according to Claim 22 wherein the  
immunoregulatory abnormality is rheumatoid arthritis

28. The method according to Claim 22 wherein the  
15 immunoregulatory abnormality is systemic lupus erythematosus

29. The method according to Claim 22 wherein the  
immunoregulatory abnormality is psoriasis

30. The method according to Claim 22 wherein the  
20 immunoregulatory abnormality is rejection of transplanted organ or tissue

31. The method according to Claim 22 wherein the  
immunoregulatory abnormality is inflammatory bowel disease.  
25

32. The method according to Claim 22 wherein the  
immunoregulatory abnormality is a malignancy of lymphoid origin.

33. The method according to Claim 22 wherein the  
30 immunoregulatory abnormality is acute and chronic lymphocytic leukemias and lymphomas.

34. A method of suppressing the immune system in a mammalian  
patient in need of immunosuppression comprising administering to said patient an  
35 immunosuppressing effective amount of a compound of Claim 1.

35. A pharmaceutical composition comprised of a compound in accordance with Claim 1 in combination with a pharmaceutically acceptable carrier.